

This listing of claims will replace all prior versions and listings of claims in the application:

**Listing of Claims:**

1-18. (cancelled)

19. (original) A method of reducing insulin resistance in a mammalian patient comprising administering a suitable phosphodiesterase antagonist.

20. (original) The method of claim 19 wherein the insulin resistance is HISS-dependent insulin resistance.

21. (original) A method of amplifying the effect of nitric oxide on skeletal muscle insulin sensitivity comprising administering a phosphodiesterase antagonist.

22. (original) A method of increasing glucose uptake by skeletal muscle of a patient, comprising administering a phosphodiesterase antagonist.

23. (currently amended) The method of ~~one of claims 19~~ claim 19, wherein the antagonist is at least one of vinpocetine, zaprinast and dipyridamole, sildenafil, theophylline, aminophylline, isobutylmethyl xanthine anagrelide, tadalafil, dyphylline, vardenafil, cilostazol, caffeine, milrinone, amrinone pimobendan, cilostamide, enoximone, teroximone, vesmarinone, rolipram ~~and~~ or R020-1724.

24. (currently amended) The method of claim 23 wherein the antagonist is at least one of vinpocetine, zaprinast and dipyridamole, sildenafil, theophylline, aminophylline, isobutylmethyl xanthine anagrelide, tadalafil, dyphylline, vardenafil, cilostazol ~~and~~ or caffeine.

25. (currently amended) The method of ~~any one of claims 19~~ claim 19, wherein the phosphodiesterase antagonist is an antagonist of at least one of phosphodiesterase of subtype 3 and subtype 5.

26. (currently amended) The method of claim ~~4~~ 19 further comprising administering at least one other drug used in the treatment of diabetes.

27. (currently amended) The method of claim 26 wherein the other drug is at least one of insulin, insulin analogues, sulfonylurea agents, tolbutamide, acetohexamide, tolazamide, chlorpropamide, glyburide, glipizide, glimepiride, biguanide agents, metformin, alpha-glucosidase inhibitors, acarbose, miglitol, thiazolidinedione agents (insulin sensitizers), rosiglitazone, pioglitazone, troglitazone, meglitinide agents, repaglinide, cholinesterase inhibitors, donepezil, tacrine, edrophonium, demecarium, pyridostigmine, phospholine, metrifonate, neostigmine, galanthamine, zanapezil, cholinergic agonists, acetylcholine, methacholine, bethanechol, carbachol, pilocarpine hydrochloride, nitric oxide donors, products or processes to increase NO synthesis in the liver (increasing NO synthase activity), SIN-1, molsidamine, N-acetylcysteine, cysteine esters, L-2-oxothiazolidine-4-carboxylate (OTC), gamma glutamylcystein and its ethyl ester, glutathione ethyl ester, glutathione isopropyl ester, lipoic acid, cysteine, cystine, methionine, S-adenosylmethionine, products or processes to reduce the rate of NO degradation in the liver, products or processes to provide exogenous NO or an exogenous carrier or precursor which is taken up and releases NO in the liver, antioxidants, vitamin E, vitamin C, 3-morpholinostyrene, glutathione increasing compounds, N-acetylcysteine, cysteine esters, L-2-oxothiazolidine-4-carboxylate (OTC), gamma glutamylcystein and its ethyl ester, glutathione ethyl ester, glutathione isopropyl ester, lipoic acid, cysteine, cystine, methionine, ~~and~~ or S-adenosylmethionine.

28. (currently amended) The method of claim ~~4~~ 19, wherein the phosphodiesterase antagonist is preferentially targeted to the liver.

29. (currently amended) The method of claim 28 19, wherein the phosphodiesterase antagonist is ~~targeted~~ bound to ~~the liver using~~ albumin.

30. (currently amended) The method of claim 28 19, wherein the phosphodiesterase antagonist is ~~targeted to the liver using a plurality of liposomes~~ incorporated into or encapsulated within liposomes.

31. (currently amended) The method of claim 28 19, wherein the phosphodiesterase antagonist bound is ~~targeted~~ to ~~the liver using~~ bile salts.

32. (previously presented) The method of claim 19, wherein the phosphodiesterase antagonist is administered by intravenous administration.

33. (previously presented) The method of claim 19, wherein the phosphodiesterase antagonist is administered by transdermal administration.

34. (previously presented) The method of claim 19, wherein the phosphodiesterase antagonist is administered by oral administration.

35. (currently amended) The method of claim 19, wherein the phosphodiesterase antagonist is administered by ~~intra-peritoneal~~ intraperitoneal administration.

36. (previously presented) The method of claim 19, wherein the phosphodiesterase antagonist is administered by portal vein injection.

37. (previously presented) The method of claim 19, wherein the phosphodiesterase antagonist is administered orally at a dose of between about 2 and 300 mg/kg body weight.

38. (previously presented) The method of claim 19, wherein the phosphodiesterase antagonist is administered intravenously at a dose of between about 5 and 500 µg/kg body weight.

39. (currently amended) The method of claim ~~19~~ 19, wherein the patient suffers from at least one of: chronic liver disease, chronic hypertension, type II diabetes, fetal alcohol syndrome, gestational diabetes, obesity, age-related insulin resistance, ~~and~~ or hepatic nerve damage.

40. (currently amended) The method of claim ~~19~~ 19, wherein the patient is a human.

41-46. (cancelled)

47. (currently amended) The method of one of claims 21 wherein the phosphodiesterase antagonist is at least one of vinpocetine, zaprinast and dipyridamole, sildenafil, theophylline, aminophylline, isobutylmethyl xanthine anagrelide, tadalafil, dyphylline, vardenafil, cilostazol, caffeine, milrinone, amrinone pimobendan, cilostamide, enoximone, teroximone, vesmarinone, rolipram and R020-1724.

48. (currently amended) The method of one of claims 22 wherein the phosphodiesterase antagonist is at least one of vinpocetine, zaprinast and dipyridamole, sildenafil, theophylline, aminophylline, isobutylmethyl xanthine anagrelide, tadalafil, dyphylline, vardenafil, cilostazol, caffeine, milrinone, amrinone pimobendan, cilostamide, enoximone, teroximone, vesmarinone, rolipram ~~and~~ or R020-1724.

49. (currently amended) The method of any one of claims 21, wherein the phosphodiesterase antagonist is ~~an antagonist of~~ at least one of phosphodiesterase of subtype 3 ~~and~~ or subtype 5.

50. (currently amended) The method of any one of claims 22, wherein the phosphodiesterase antagonist is ~~an antagonist of~~ at least one of phosphodiesterase of subtype 3 ~~and~~ or subtype 5.

51. (previously presented) The method of claim 21, wherein the phosphodiesterase antagonist is administered by intravenous administration.

52. (previously presented) The method of claim 22, wherein the phosphodiesterase antagonist is administered by intravenous administration.

53. (previously presented) The method of claim 21, wherein the phosphodiesterase antagonist is administered by transdermal administration.

54. (previously presented) The method of claim 22, wherein the phosphodiesterase antagonist is administered by transdermal administration.

55. (previously presented) The method of claim 21, wherein the phosphodiesterase antagonist is administered by transdermal administration.

56. (previously presented) The method of claim 22, wherein the phosphodiesterase antagonist is administered by transdermal administration.

57. (previously presented) The method of claim 21, wherein the phosphodiesterase antagonist is administered by intra peritoneal administration.

58. (previously presented) The method of claim 22, wherein the phosphodiesterase antagonist is administered by intra peritoneal administration.

59. (previously presented) The method of claim 21, wherein the phosphodiesterase antagonist is administered by portal vein injection.

60. (previously presented) The method of claim 22, wherein the phosphodiesterase antagonist is administered by portal vein injection.

61. (previously presented) The method of claim 21, wherein the phosphodiesterase antagonist is administered orally at a dose of between about 2 and 300 mg/kg body weight.

62. (previously presented) The method of claim 22, wherein the phosphodiesterase antagonist is administered orally at a dose of between about 2 and 300 mg/kg body weight.

63. (previously presented) The method of claim 21, wherein the phosphodiesterase antagonist is administered intravenously at a dose of between about 5 and 500  $\mu$ g/kg body weight.

64. (previously presented) The method of claim 22, wherein the phosphodiesterase antagonist is administered intravenously at a dose of between about 5 and 500  $\mu$ g/kg body weight.